REMARKS

I. Status of the Claims

Claims 1-27 and 33 are pending in the application. New claims 34-50 are added herein. Applicants request consideration of these claims, as well as those advanced in the previous response.

II. Rejections Under 35 U.S.C. §112, First Paragraph

Claims 1-27 were rejected, and the specification was objected to, as the disclosure allegedly lacks enabling support for the claimed invention. Applicants provide the following comments, with respect to the new claims, to the extent that the rejection was applied to subject matter thereof.

With respect to allegations that the specification does not contain adequate information on virus doses and routes, applicants merely refer to the examiner to the previous response. Similarly, in response to the general attack on gene therapy, applicants point to their submitted comments. With respect to the issue of scope, applicants respectfully submit that the specification enables more than just the use of herpesviruses.

Example II is directed to the use of adenovirus, in combination with ionizing radiation, to treat animals bearing human tumors. This example shows that adenoviral vectors, whether containing a TNF gene, a *lac*Z gene or no exogenous gene, were able to cause regression of tumors beyond that seen with ionizing radiation alone. It is important to note that there was no

significant difference between these three viral vectors with respect their anti-tumor effect, indicating that the particular vector was not critical to the phenomenon. Thus, it is submitted that the rejection, as framed against the previous claims, should not be proper here.

III. Rejection Under 35 U.S.C. §102

Previously, claims 1-3, 6, 8, 9, 12, 23-25 and 27 were rejected under §102 over Fujiwara *et al.* ("Fujiwara"). Fujiwara was said to disclose adenoviral-mediated transfection of cancer cells prior to administration of a DNA damaging composition. Further, claims 1-27 were rejected as obvious over Wills *et al.* ("Wills"), taken with Fujiwara and Boviatis.

With respect to the anticipation rejection, applicants simply submit that the Fujiwara work involved the use of an adenovirus carrying exogenous therapeutic gene encoding the p53 tumor suppressor. The new claims provided here specifically exclude the use of an exogenous therapeutic gene and, thus, do not run afoul of the Fujiwara reference.

As for the obviousness rejection, applicants again point out that neither Wills, nor Boviatis nor Fujiwara presage the present invention, which relies only on the use of adenoviral vectors and does not rely on the use of exogenous therapeutic genes expressed therefrom. Wills, like Fujiwara, discloses an adenoviral vector carrying a gene for p53, and hence does not address the present invention. Additionally, comments regarding CTL destruction and viral-mediated cytotoxicity are not well taken given that there was no difference seen in the effects on control-treated tumors and tumors being treated with adenovirus alone (Specification at page 29, lines 6-

11). Moreover, it is submitted that the ability of adenoviral-null and adenoviral-*lac*Z vectors to cause tumor regression equivalent to that of an adenoviral-TNF vector was completely unexpected (Specification at page 30, line 4-15). Thus, for all of the foregoing reasons, applicants respectfully submit that the newly submitted claims also are non-obvious.

IV. Conclusion

Applicants submit that the new claims, like those submitted previously, are in condition for allowance. Should Examiner Milne have any questions regarding this response, he is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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